



General

Guideline Title

American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer.

Bibliographic Source(s)

Smallridge RC, Ain KB, Asa SL, Bible KC, Brierley JD, Burman KD, Kebebew E, Lee NY, Nikiforov YE, Rosenthal MS, Shah MH, Shaha AR, Tuttle RM, American Thyroid Association Anaplastic Thyroid Cancer Guidelines Taskforce. American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. *Thyroid*. 2012 Nov;22(11):1104-39. [235 references] [PubMed](#)

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Quality of evidence (High, Moderate, Low, Insufficient for grading) and strength of recommendations (Strong, Weak, None) are defined at the end of the "Major Recommendations" field.

Diagnosis: Histopathology and Differential Diagnosis

Differential Diagnosis

Recommendation 1. Morphologic diagnosis with appropriate immunostaining as relevant is mandatory to exclude other less aggressive and treatable entities that can mimic anaplastic thyroid cancer (ATC). Strength of Recommendation: Strong, Quality of Evidence: Moderate

Cytology and Pathology Procedures

Recommendation 2. Fine-needle aspiration (FNA) cytology or core biopsy should play a role in the preoperative diagnosis of ATC. In cases in which the limited sampling of FNA or core biopsy yields material that is nondiagnostic, open biopsy should be performed to obtain diagnostic tissue. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 3. Whenever possible, a definitive diagnosis should be obtained prior to surgery. Intraoperative pathology consultation can be used to define the adequacy of the resected tissue for diagnostic evaluation or to identify ATC in a patient when that diagnosis was not anticipated preoperatively. Intraoperative pathology consultation is not usually appropriate for definitive diagnosis. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 4. Pathological evaluation should provide information on the proportion of tumor that comprises ATC and coexistent well-differentiated or poorly differentiated thyroid carcinoma, which may affect prognosis and guide management. Strength of Recommendation: Strong

Quality of Evidence: Low

Recommendation 5. Molecular studies based on deoxyribonucleic acid/ribonucleic acid (DNA/RNA) analysis are not currently required for diagnosis and management of patients with ATC. Strength of Recommendation: Strong, Quality of Evidence: Moderate

Initial Evaluations

Laboratory, Biopsy, and Imaging Procedures

Recommendation 6. Adjunctive preoperative radiological tumor staging should not delay therapy and should make use of appropriate cross-sectional imaging including neck ultrasound, computed tomography (CT) scans or magnetic resonance imaging (MRI) (for the neck and chest), and positron emission tomography (PET)/CT fusion scans. Strength of Recommendation: Strong, Quality of Evidence: Moderate

Recommendation 7. Primary management of ATC should not be delayed in order to biopsy tumors at distant sites. If clinically indicated, such biopsies could be performed after completion of primary surgery. Strength of Recommendation: Weak, Quality of Evidence: Low

Timing and Nature of Evaluation Studies

Recommendation 8. All critical appointments and assessments that are required prior to primary treatment of ATC should be prioritized and completed as rapidly as possible. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 9. Every patient should undergo initial evaluation of the vocal cords. The best way to evaluate the vocal cords is with fiber optic laryngoscopy; however, mirror examination may be acceptable. Fiber optic laryngoscopy will also help to assess the opposite vocal cord, mobility of the vocal cord, and endolaryngeal pathology and whether there is any extension of disease in the subglottic or upper tracheal area. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 10. Only imminently threatening disease elsewhere (e.g., brain or spine metastases or pulmonary hemorrhage) should prevent primary surgical management of neck disease if achievable. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 11. If preoperative staging and primary tumor assessment define the tumor extent as precluding safe or effective surgical resection, neoadjuvant external beam radiotherapy and/or chemotherapy should be considered to permit delayed primary surgical resection. Strength of Recommendation: Strong, Quality of Evidence: Moderate

Postdiagnostic Care of ATC

Recommendation 12. A comprehensive multimodality management plan should be rapidly formulated and implemented by a multidisciplinary thyroid cancer management team. Strength of Recommendation: Strong, Quality of Evidence: Low

Prognostic Factors

Recommendation 13. ATC is an aggressive tumor with a poor prognosis and high mortality. Assessment of predictive factors such as age, sex, tumor size, histology, and clinical stage should be performed in all patients. Strength of Recommendation: Strong, Quality of Evidence: Moderate

Establishing Treatment Goals

Treatment and Care Goals

Recommendation 14. Physicians involved with the management decisions in the care of the patient should consult with multidisciplinary specialists who may be involved in the care of the patient, either at the present time or in the future, before having "goals of care" discussions with patients. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 15. Patients must have decision-making capacity to consent to or make particular medical decisions. Concerns about diminished or impaired capacity may prompt a psychiatric consult or clinical ethics consult to assess barriers to capacity. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 16. If patients require a surrogate (proxy) decision maker, the treating physician should ensure that one is appointed according to the patient's stated preferences if known (written or verbal) or in compliance with local jurisdiction laws surrounding surrogacy and guardianship in consultation with a hospital ethicist or attorney. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 17. In consultation with a multidisciplinary team (see Recommendation 14), a candid meeting with the patient should be scheduled in which there is full disclosure of the potential risks and benefits of various treatment options, including how such options will impact the patient's life. Treatment options discussed should include palliative care. Patient preferences should guide clinical management. Strength of

Recommendation: Strong, Quality of Evidence: Low

Recommendation 18. Patients should be encouraged to draft an advance directive in which they name a surrogate decision maker and list code status and other end-of-life preferences. Consider, in some cases, using "allow natural death" (AND) over "do not resuscitate" (DNR), which may be better understood by patients and families as an order that limits inappropriate aggressive care. Circumstances in which suspension of DNR or AND may occur must be discussed with the patient. Strength of Recommendation: Strong, Quality of Evidence: Low

Approaches to Locoregional Disease

Roles of Surgery

Recommendation 19. Resectability of ATC should be determined by routine preoperative imaging studies (ultrasound, CT, MRI, and/or PET scan of the neck and chest). If locoregional disease is present and a grossly negative margin (R1 resection) can be achieved, surgical resection should be considered. In patients with systemic disease, resection of the primary tumor for palliation should be considered to avoid current or eventual airway or esophageal obstruction. Strength of Recommendation: Strong, Quality of Evidence: Moderate

Recommendation 20. A total lobectomy or total or near-total thyroidectomy with a therapeutic lymph node dissection should be performed in patients with intrathyroidal ATC. Strength of Recommendation: Strong, Quality of Evidence: Moderate

Recommendation 21. In patients with extrathyroidal invasion, an en bloc resection should be considered if grossly negative margins (R1 resection) can be achieved. Strength of Recommendation: Strong, Quality of Evidence: Moderate

Recommendation 22. A total lobectomy or total or near-total thyroidectomy should be performed in most patients with an incidental area of ATC within a differentiated thyroid cancer (DTC). This is based primarily on treatment recommendations related to the non-anaplastic component of the malignancy. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 23. The data are inadequate to definitively recommend either for or against local or systemic adjuvant therapy for small, intrathyroidal ATCs. A majority of the authors would favor cautious observation with frequent anatomic imaging studies for at least the first year of follow-up, while a minority would recommend adjuvant therapy. Strength of Recommendation: Weak, Quality of Evidence: Low

Recommendation 24. Every attempt should be made to identify the contralateral recurrent laryngeal nerve, especially if the ipsilateral nerve is paralyzed, to protect the nerve from injury, which may lead to bilateral vocal cord paralysis and requirement for tracheostomy. A nerve monitor may be quite helpful to confirm nerve function. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 25. Patients with ATC may require tracheostomy to avoid asphyxia. It should be done in an operating room setting, unless acute airway distress demands immediate action. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 26. The patient's airway should be closely monitored in the recovery room during the postoperative period and throughout radiation therapy. Elective tracheostomy is best avoided unless there are acute airway issues. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 27. Tracheostomy may be temporarily beneficial in patients with impending airway loss. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 28. Tracheostomy or stent placement is best avoided unless there is impending airway compromise. Strength of Recommendation: Strong, Quality of Evidence: Low

Radiotherapy and Systemic Chemotherapy in Locoregional ATC

Recommendation 29. Following an R0 or R1 resection (excluding an incidental intrathyroidal microscopic lesion; see Recommendation 23), patients with good performance status with no evidence of metastatic disease who wish an aggressive approach should be offered definitive radiation therapy (with or without concurrent chemotherapy, see Recommendation 36). Strength of Recommendation: Strong, Quality of Evidence: Moderate

Recommendation 30. Treatment should be planned and radiation started as soon as the patient is sufficiently recovered from neck surgery, usually within 2 to 3 weeks after surgery. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 31. Systemic chemotherapy can begin as soon as the patient is sufficiently recovered from surgery, potentially even within 1 week of surgery, depending upon postoperative course and treatment goals. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 32. Patients who have undergone R2 resection or have unresected disease with good performance status and who wish an

aggressive approach should be offered definitive radiation (with or without concurrent chemotherapy; see Recommendation 36). Strength of Recommendation: Strong, Quality of Evidence: Moderate

Recommendation 33. Surgical resection may be reconsidered in patients when radiation (with or without chemotherapy) renders the tumor potentially resectable. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 34. Patients with local symptoms and poor performance status should be offered palliative radiotherapy. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 35. Patients who are to receive radiation for unresectable thyroid cancer or in the postoperative setting should, where available, be treated with intensity-modulated radiotherapy (IMRT); however, treatment should not be delayed because of lack of availability of IMRT. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 36. The use of cytotoxic chemotherapy involving some combination of taxane (paclitaxel or docetaxel), and/or anthracyclines (doxorubicin) and/or platin (cisplatin or carboplatin) therapy should be considered in combination with radiation therapy or altered fractionated radiotherapy in good performance status patients with nonmetastatic ATC who desire aggressive therapy. Strength of Recommendation: Strong, Quality of Evidence: Moderate

Supportive Care During Active Therapy

Recommendation 37. In the absence of impending airway compromise, minor airway-related issues can be overcome with humidity, rest, and occasional use of short-term corticosteroids. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 38. If the patient with ATC has difficulty swallowing and treatment with surgery, radiation, or chemoradiation therapy is planned, gastrostomy for enteral nutrition should be considered. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 39. A percutaneous endoscopic gastrostomy (PEG) tube may be difficult to place if the patient has involvement or obstruction of the esophagus. A percutaneous radiologically-directed gastrostomy may be indicated in these patients. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 40. Total parenteral nutrition is rarely necessary in patients with ATC. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 41. The use of preemptive granulocyte colony-stimulating growth factor/pegfilgrastim or weekly chemotherapy dosing regimens should be strongly considered when combining chemotherapy and radiotherapy in ATC so as to minimize the risks of treatment-related neutropenia and neutropenic infections. Strength of Recommendation: Strong, Quality of Evidence: Low

Approaches to Advanced Metastatic Disease (Stage IVC)

Timing of Systemic Therapies

Recommendation 42. Palliation of symptomatic and/or imminently threatening lesions should be given high priority in comparison to treatment with systemic therapy unless the primary threat to the patient is diffuse disease progression. Strength of Recommendation: Strong, Quality of Evidence: Low

Approaches to Systemic Disease (Novel or Investigational)

Recommendation 43. Since systemic therapy can result in transient, and occasionally more durable, disease regression or control in patients with advanced ATC and may improve survival in responders, it can reasonably be considered in patients with metastatic ATC of good performance status wishing an aggressive approach. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 44. Patients with advanced or metastatic ATC wishing an aggressive approach should be encouraged to participate in clinical trials given the rarity of ATC, lack of data in support of improved survival or quality of life from any systemic therapeutics, and the need to develop evidence-based safe and effective therapeutic approaches in advanced ATC. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 45. Combination or monotherapy including a taxane and/or an anthracycline could be considered in metastatic ATC if a suitable clinical trial is not otherwise available. Strength of Recommendation: Strong, Quality of Evidence: Moderate

Recommendation 46. Since aggressive tumor-directed therapy may not be desired by or appropriate for all patients with metastatic ATC, consideration of best supportive care or hospice should also be prominently discussed as an alternative to systemic cancer-directed therapy. Strength of Recommendation: Strong, Quality of Evidence: Low

Approaches to Brain Metastases

Recommendation 47. Patients considering therapy should have radiologic studies (MRI or CT scan) assessing the presence of brain metastases when ATC is diagnosed. Additional radiologic studies of the brain are indicated in the context of progressive disease and/or neurological abnormalities suggesting the development of a brain lesion or change in character or size of a known brain lesion. Strength of Recommendation: Strong, Quality of Evidence: Moderate

Recommendation 48. Surgical removal of brain lesion(s) in selected patients and/or radiation therapy may result in better disease control. Strength of Recommendation: Weak, Quality of Evidence: Low

Recommendation 49. Neurologically asymptomatic patients with brain metastases do not routinely require exogenous corticosteroid administration. Patients with neurologic brain compressive symptoms or signs should preferably receive dexamethasone (or alternatively a glucocorticoid equivalent) at appropriate doses. Individual patient considerations should apply with regard to the initiation, dose, and duration of exogenous corticosteroid administration. Strength of Recommendation: Strong, Quality of Evidence: Moderate

Recommendation 50. It is not recommended that patients with brain metastases from ATC routinely receive prophylactic antiseizure medications. Strength of Recommendation: Weak, Quality of Evidence: Low

Approaches to Bone Metastases

Recommendation 51. Patients with ATC who during the course of monitoring and treatment have skeletal symptoms, such as pain or pathologic fracture, should have radiologic evaluation of the specific area of concern. If there is proven osseous metastasis at a single specific site, radiologic evaluation of the skeleton may be performed to identify other sites of bony metastases. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 52. It is reasonable to treat osseous metastases from ATC in a comparable manner to patients with other aggressive tumors causing osseous metastases with emphasis on radiotherapy and/or surgery. Metastatic lesions to the bone should be considered for palliative radiotherapy. If the lesions are in a weight-bearing region, orthopedic fixation should be considered prior to initiation of palliative radiotherapy. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 53. Patients with known osseous metastases from ATC should be considered for periodic intravenous bisphosphonate infusions or subcutaneous receptor activator of nuclear factor B ligand (RANK ligand) inhibitor. Given the lack of data, it is not possible to make a definitive recommendation regarding the frequency and duration of these treatments. Strength of Recommendation: Weak, Quality of Evidence: Low

Utility of Cryoablation and Selective Embolization

Recommendation 54. A definitive recommendation regarding cryoablation, radiofrequency ablation, and selective embolization in patients with ATC cannot be made. Strength of Recommendation: Weak, Quality of Evidence: Insufficient

Approach to Thrombosis and/or Tumor Invasion into Vasculature

Recommendation 55. Tumor invasion into cervical veins can be diagnosed by CT, MRI, or venogram in the appropriate clinical context. There are insufficient data available to recommend either monitoring or a specific therapy such as surgery or radiation therapy for vascular tumor invasion. Strength of Recommendation: Weak, Quality of Evidence: Low

Recommendation 56. Consider prophylactic anticoagulation in patients who are at high risk for thromboembolic disease such as major surgery or receiving pertinent chemotherapy (specifically including thalidomide or lenalidomide). Strength of Recommendation: Strong, Quality of Evidence: Moderate

Recommendation 57. Patients with documented venous thromboembolism should generally be treated with low molecular weight heparin with specific consideration of the individual context. Strength of Recommendation: Strong, Quality of Evidence: High

Palliative Care and Hospice

Definition of a Palliative Care Service

Recommendation 58. The treatment team should include palliative care expertise at every appropriate stage of patient management to help with pain and symptom control, as well as addressing psychosocial and spiritual issues. Palliative care services are appropriate for any ATC patient receiving treatment intended to prolong life. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 59. The treatment team should engage hospice care for ATC patients who decline therapies intended to prolong life, yet still

require symptom and pain relief spanning the remainder of their illness. Strength of Recommendation: Strong, Quality of Evidence: Low

Surveillance and Long-term Monitoring

Surveillance after Clinical Remission

Recommendation 60. Following initial staging and therapy, patients without evidence for persistent structural disease desiring ongoing aggressive management should have cross-sectional imaging of the brain, neck (and/or ultrasound), chest, abdomen, and pelvis at 1- to 3-month intervals for 6–12 months, then at 4- to 6-month intervals for a minimum of 1 additional year. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 61. ^{18}F -fluorodeoxyglucose (^{18}FDG) PET scanning should be considered about 3–6 months after initial therapy in patients with no clinical evidence of disease to identify small volume disease that may require a change in the management plan. Furthermore, ^{18}FDG PET scanning should also be considered at 3- to 6-month intervals in patients with persistent structural disease as a guide to the response to therapy and to identify new sites of disease that may necessitate a change in the management plan. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 62. Neither serum thyroglobulin (Tg) measurements nor radioactive iodine (RAI) scanning or therapy are recommended in the initial management of ATC unless the anaplastic component represents a minor component of a more well-differentiated thyroid cancer. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 63. After a 6- to 12-month follow-up period, patients without evidence of recurrent/progressive ATC should be considered for RAI therapy if the original tumor had well-differentiated thyroid cancer components. Strength of Recommendation: Strong, Quality of Evidence: Low

Restaging of Patients with Persistent Metastatic Disease

Recommendation 64. Patients with persistent structural disease following initial staging and therapy should have frequent cross-sectional imaging (at least every 1–3 months), which may include brain, neck, chest, abdomen, pelvis, and known sites of disease as clinically indicated to guide systemic and/or local therapy. Strength of Recommendation: Strong, Quality of Evidence: Low

Recommendation 65. Patients with persistent structural disease following initial staging and therapy who wish to minimize additional therapy may undergo symptom-directed cross-sectional imaging. Strength of Recommendation: Strong, Quality of Evidence: Low

Definitions:

Quality of Evidence

High – Requires one or more randomized, controlled trials without important limitations, or overwhelming evidence from observational studies

Moderate – Derived from trials with important limitations, or exceptionally strong observational studies

Low – Supported only by observational studies or case series

Insufficient for grading – Evidence is lacking, of poor quality, or conflicting

Strength of Recommendations

Strong – Benefits clearly outweigh risks and burden, *or* risks and burden clearly outweigh benefits

Weak – Benefits finely balanced with risks and burden

None – Insufficient evidence to determine net benefits or risks

Clinical Algorithm(s)

The original guideline document includes clinical algorithms on the following topics:

- Anaplastic thyroid carcinoma management options
- Stage IVA or IVB tumor resectable: Initial therapy and follow-up
- Stage IVB tumor unresectable: Initial therapy and follow-up
- Stage IVC: Establish goals and initial therapy

Scope

Disease/Condition(s)

Anaplastic thyroid cancer

Guideline Category

Diagnosis

Evaluation

Management

Risk Assessment

Treatment

Clinical Specialty

Endocrinology

Family Practice

Internal Medicine

Nuclear Medicine

Oncology

Otolaryngology

Pathology

Radiation Oncology

Radiology

Surgery

Intended Users

Advanced Practice Nurses

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

To provide a comprehensive set of guidelines to assist practitioners in the management of critically ill patients with anaplastic thyroid cancer

Target Population

Patients with known, or suspected, anaplastic thyroid cancer

Interventions and Practices Considered

Diagnosis/Evaluation/Risk Assessment

1. Morphologic diagnosis with immunostaining as relevant
2. Fine-needle aspiration (FNA), core biopsy, or open biopsy
3. Intraoperative pathology consult, when needed
4. Tumor staging using cross-sectional imaging, including neck ultrasound, computed tomography (CT) scans, magnetic resonance imaging (MRI), positron emission tomography (PET)/CT fusion scans
5. Evaluation of vocal cords with fiber optic laryngoscopy or mirror evaluation
6. Assessment of predictive factors (age, sex, tumor size, histology, clinical stage)

Treatment/Management

1. Neoadjuvant external beam radiotherapy and/or chemotherapy when primary assessment of tumor precludes safe or effective surgical resection
2. Comprehensive multimodal management plan, including consultation with specialists
3. Discussion of goals of care, risks and benefits of treatment options, and advance directives with patient
4. Psychiatric consult or clinical ethics consult and appointment of surrogate decision maker, as appropriate
5. Surgery
 - Total lobectomy or total or near-total thyroidectomy with therapeutic lymph node dissection
 - En bloc resection
 - Tracheostomy, as required to avoid asphyxia
6. Radiotherapy with or without chemotherapy
7. Supportive care
 - Airway management, including humidity, rest, and short-term corticosteroids
 - Gastrostomy for enteral nutrition
 - Preemptive granulocyte colony-stimulating growth factor/pegfilgrastim or weekly chemotherapy dosing regimens
8. Management of advanced metastatic disease
 - Palliation of symptomatic and/or threatening lesions
 - Systemic therapy (combination or monotherapy including a taxane and/or an anthracycline)
 - Best supportive care or hospice
 - Assessment for and management of metastases (brain, bone, or other)
9. Surveillance and long-term monitoring, including periodic imaging

Major Outcomes Considered

- Histopathological features of anaplastic thyroid cancer
- Accuracy, sensitivity, and specificity of diagnostic procedures
- Efficacy/effectiveness of treatment/management strategies
- Prognostic value of markers
- Median, 1-year, 2-year, 5-year, disease-free, and overall survival
- Long-term disease control
- Morbidity
- Mortality
- Palliative benefit of interventions
- Levels of pain
- Quality of life
- Adverse effects and toxicity of treatment/management strategies

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

To identify all literature that might assist in preparing this document, a PubMed search of the terms "anaplastic thyroid cancer," "anaplastic thyroid carcinoma," and "anaplastic thyroid" was performed. A total of 2,157 articles were identified. A search of "ATC and randomized clinical trials" was also performed and yielded no publications. The literature search extended from 2009 into 2012.

Number of Source Documents

2157 articles were reviewed.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Quality of Evidence

High – Requires one or more randomized, controlled trials without important limitations, or overwhelming evidence from observational studies

Moderate – Derived from trials with important limitations, or exceptionally strong observational studies

Low – Supported only by observational studies or case series

Insufficient for grading – Evidence is lacking, of poor quality, or conflicting

Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

To rank the quality of the evidence supporting a recommendation, the Taskforce used the criteria described in the "Rating Scheme for the Strength of the Evidence" field. These criteria were adapted from the Clinical Guidelines Committee of the American College of Physicians, which in turn were developed by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) workgroup.

For anaplastic thyroid cancer, the extent of surgical resection has been implicated as a prognostic factor by many authors. Therefore, the American Joint Committee on Cancer Cancer Staging Manual (7th edition) Residual Tumor (R) Classification was used to assess surgical effects on outcomes across the studies reviewed (see Table 3 in the original guideline document).

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The American Thyroid Association (ATA) Board of Directors requested that an independent Taskforce develop a more comprehensive set of guidelines to assist practitioners in the management of critically ill patients with anaplastic thyroid cancer (ATC). The authors include physicians

who specialize in endocrinology, endocrine surgery, head/neck surgery, nuclear medicine, radiation oncology, medical oncology, pathology, and bioethics.

In preparing the guidelines, the Taskforce developed a list of questions covering the areas of diagnosis, initial evaluation, establishing treatment goals, approaches to locoregional disease, approaches to advanced/metastatic disease, palliative care/hospice, and surveillance and long-term monitoring. To maximize deliberations, the Taskforce developed preliminary recommendations and solicited input from the ATA Board of Directors and members of the ATA by posting them on the members-only section of the ATA website (www.thyroid.org). All responses were from ATA members. Final recommendations, the strength of the recommendation, and the quality of the evidence were arrived at by consensus of the authors.

To rank the strength of each recommendation, the Taskforce used the criteria described in the "Rating Scheme for the Strength of the Recommendations" field. These criteria were adapted from the Clinical Guidelines Committee of the American College of Physicians, which in turn were developed by the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) workgroup. Given the rarity of ATC and lack of funding to support prospective trials, the types of publications are mostly low-quality. However, the authors consider that they were frequently able to make strong recommendations.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Strong – Benefits clearly outweigh risks and burden, *or* risks and burden clearly outweigh benefits

Weak – Benefits finely balanced with risks and burden

None – Insufficient evidence to determine net benefits or risks

Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

The final document was approved by the American Thyroid Association (ATA) Board of Directors, and was officially endorsed by 10 organizations. Please refer to the "Guideline Endorser(s)" field for an alphabetical listing.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Potential Harms

What constitutes clinical harms in anaplastic thyroid cancer (ATC) management may be highly variable and can depend on a range of circumstances such as the patient's age, comorbid conditions, tumor status, overall health, and psychosocial support system.

Locoregional Disease

- The patients with ATC who require tracheostomy have advanced local disease, and the chances of long-term survival are quite small. Under these circumstances, the tracheostomy may prolong some suffering. Tracheostomy does lead to secretions, need for frequent suctioning, and overall discomfort that the patient may experience.
- In patients with initially unresectable disease, chemoradiation may rarely enable subsequent resection and should be considered in patients with good performance status and without metastatic disease. However, the potential benefit in a few must be weighed against the risk of toxicity in a population of patients, the majority of whom still have a poor survival.
- The addition of chemotherapy to radiation therapy has potential to increase morbidity and potentially mortality.
- The toxicities associated with high-dose radiotherapy concurrent with chemotherapy are seen both in the acute and late setting. During chemotherapy and radiotherapy, patients' major complaints are dysphagia and odynophagia. Severe mucous production giving rise to a "choking" sensation and desquamation of the skin are also common side effects. The difficulty in swallowing can result in the placement of a percutaneous endoscopic gastrostomy (PEG) tube. At this time, the treating physician should continue to counsel patients to swallow because the discontinuation of swallowing can result in PEG tube dependence. This is the major late complication associated with high-dose radiotherapy, and hence every effort to counsel patients to continue swallowing during radiotherapy is warranted.
- During active treatment some existing patient risks are increased, while other new risks arise. The patient, family, and involved health care providers must be fully informed about these risks, with risk mitigation plans articulated.
- Patients with ATC undergoing radiation therapy require close monitoring. The airway may become narrowed from the effect of ATC, vocal cord paralysis, or endolaryngeal edema due to radiation therapy.
- Adding chemotherapy to radiation therapy, with the aims of improving disease control in irradiated areas and, in parallel, preemptively treating microscopic metastatic disease, has the potential to increase toxicity. Among the most serious potential toxicities from chemotherapy is that of infection complicating chemotherapy-induced neutropenia; this risk is heightened by the concomitant use of chemotherapy and radiation. Further, mucositis or esophagitis is commonly induced by intensive radiotherapy, resulting in disruption of some of the usual mucosal defenses against infection. Collectively, these factors result in an inordinate risk of serious infection when combining chemotherapy with radiotherapy in ATC.

Advanced Metastatic Disease - Bone Metastasis

Bisphosphonates, especially given intravenously, have potential side effects that include an acute-phase reaction and post-therapy bony pains, hypocalcemia, and rarely osteonecrosis of the jaw. There is also a risk of atypical femoral fractures, but this risk is small compared to benefits in patients with bony metastases. Bisphosphonates should be administered cautiously to patients with renal disease. Bisphosphonate dosage should also be corrected based upon renal function and dosages held for hypocalcemia.

Contraindications

Contraindications

Bisphosphonates should not be administered to patients with a creatinine clearance 35 mL/min or less or to patients with hypocalcemia, vitamin D deficiency, or a history of allergy to bisphosphonates due to potential side effects that include an acute-phase reaction and posttherapy bony pains, hypocalcemia, and rarely osteonecrosis of the jaw.

Qualifying Statements

Qualifying Statements

- The medical opinions expressed in the guidelines are those of the authors.
- In line with and echoing some of the official policy of the American Thyroid Association (ATA), the recommendations are not inclusive of all proper approaches or methods, nor exclusive of others. They do not establish a standard of care and specific outcomes are not guaranteed. The Taskforce recommends that treatment decisions be based on independent judgment of health care providers and each patient's individual circumstances. The guideline recommendations are not intended to take the place of physician judgment in diagnosing and treating particular patients. The Taskforce expects those who use the guideline to do so as an aid in clinical decision-making, with full consideration of each patient's individuality in terms of history and physical traits.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Clinical Algorithm

For information about availability, see the *Availability of Companion Documents and Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Smallridge RC, Ain KB, Asa SL, Bible KC, Brierley JD, Burman KD, Kebebew E, Lee NY, Nikiforov YE, Rosenthal MS, Shah MH, Shaha AR, Tuttle RM, American Thyroid Association Anaplastic Thyroid Cancer Guidelines Taskforce. American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. *Thyroid*. 2012 Nov;22(11):1104-39. [235 references] [PubMed](#)

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012 Nov

Guideline Developer(s)

American Thyroid Association - Professional Association

Source(s) of Funding

American Thyroid Association

Guideline Committee

American Thyroid Association Anaplastic Thyroid Cancer Guidelines Taskforce

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

Author Disclosure Statement

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Guideline Endorser(s)

American Academy of Otolaryngology - Head and Neck Surgery - Medical Specialty Society

American Association of Clinical Endocrinologists - Medical Specialty Society

American Head and Neck Society - Professional Association

Asian & Oceania Thyroid Association - Disease Specific Society

Brazilian Society of Head and Neck Surgery - Professional Association

European Thyroid Association - Disease Specific Society

International Association of Endocrine Surgeons - Professional Association

Italian Association of Clinical Endocrinologists - Medical Specialty Society

Latin American Thyroid Society - Disease Specific Society

The Endocrine Society - Professional Association

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available from the [American Thyroid Association Web site](#) .

Availability of Companion Documents

The following is available:

- American Thyroid Association guidelines for management of patients with anaplastic thyroid cancer. Supplementary data. 5 p. Available in Portable Document Format (PDF) from the [American Thyroid Association Web site](#) .

Patient Resources

None available

NGC Status

This NGC summary was completed by ECRI Institute on April 23, 2013. The information was verified by the guideline developer on May 10, 2013. This summary was updated by ECRI Institute on March 10, 2014 following the U.S. Food and Drug Administration advisory on Low Molecular Weight Heparins. This summary was updated by ECRI Institute on July 18, 2014 following the U.S. Food and Drug Administration advisory on Docetaxel.

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